

Study of Hydrogen Bonds in Crystalline 5-Nitouracil. Density Functional Theory Calculations of the O-17, N-14, and H-2 Nuclear Quadrupole Resonance Parameters

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Hydrogen bond interaction properties of backbone uracil was studied in crystalline structure of 5-nitouracil. To this aim the electric field gradient tensors were calculated at the level of density functional theory in two single (non-hydrogen bonded) and cluster (hydrogen-bonded four-molecule) models of 5-nitouracil. The electric field gradient tensors at the sites of O-17, N-14, and H-2 nuclei were converted to the experimentally measurable nuclear quadrupole resonance spectroscopy parameters, quadrupole coupling constant and asymmetry parameter. The results indicated different hydrogen bond interaction properties at the sites of various nuclei and also the protective role of -NO₂ group for contribution of O1 to hydrogen bond interactions in comparison with uracil. The density functional theory calculations were performed using GAUSSIAN 98 package employing B3LYP method and 6-311G** and 6-311++G** basis sets.

Keywords: 5-Nitouracil, Hydrogen bond, Nuclear quadrupole resonance, Density functional theory, Electric field gradient tensors

INTRODUCTION

The key role of hydrogen bond (HB) interactions in the determination and stabilization of nucleobase pairs was firstly indicated by Watson and Crick [1]. Although numerous works employing various techniques have been devoted to study HB properties in nucleic acid structures, however, nuclear quadrupole resonance (NQR) spectroscopy is among the most important and versatile techniques for the purpose [2,3]. Electric field gradient (EFG) tensors are very sensitive elements to the electronic density at the sites of quadrupole and magnetic nuclei, respectively, and are significantly influenced by HB interactions [4].

The contribution of uracil, the characteristic RNA

nucleobase, and its derivatives to HB interactions have been previously studied due to importance of 5-derivatives of uracil in pharmaceutical and biological activities in living systems [5-12]. 5-Nitouracil (5NU) is the 5-nitro derivative of uracil whose contribution to HB interactions was reported by earlier X-ray study of Kennedy *et al.* [13]. Bednarek *et al.* [14] have also reported a NMR study of some uracil 5-derivatives including 5NU; however, they did not consider the HB interactions in the quantum chemical calculations.

Present density functional theory (DFT) work studies the properties of N-H \cdots O and C-H \cdots O types of HB interaction of the backbone uracil in the reported crystalline structure of 5NU by Kennedy *et al.* [13]. The EFG tensors are calculated at the sites of oxygen, nitrogen, and hydrogen nuclei of backbone uracil in a four-molecule cluster model of 5NU including the most possible interacting molecules with the target one (Fig. 1). Table 2 exhibits the calculated EFG tensors

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at the sites of ^{17}O , ^{14}N and ^2H quadrupole nuclei in single and cluster models of 5NU which are converted to experimentally measurable NQR parameters, quadrupole coupling constants (C_Q) and asymmetry parameters (η_Q) [15].

COMPUTATIONAL ASPECTS

Model Preparation

The considered single and cluster models of 5NU representing non-hydrogen bonded and hydrogen bonded systems are created by available X-ray coordinates [13]. However, since hydrogen positions are not accurately located by X-ray, the B3LYP/6-311G** optimization was performed to optimize just the hydrogen coordinates while the other coordinates kept frozen during the process [16]. The single model includes just a one-molecule model of 5NU, however, the cluster includes the most possible HB interacting molecules with the backbone uracil of the target 5NU in a four-molecule model (Table 1 and Fig. 1).

Tensors Calculations

The B3LYP/6-311++G** calculations were performed using GAUSSIAN 98 [17] package to evaluate the EFG tensors in the one-molecule (single) and four-molecule (cluster) models of 5NU. The calculated EFG tensors at the sites of ^{17}O , ^{14}N and ^2H nuclei were converted to experimentally measurable NQR parameters, quadrupole coupling constants (C_Q) and asymmetry parameters (η_Q), using Eqs. (1) and (2) (Table 2). The quadrupole moments (Q) employed in Eq. (1) are: $Q(^{17}\text{O}) = 25.58$ mb, $Q(^{14}\text{N}) = 20.44$ mb, and $Q(^2\text{H}) = 2.86$ mb [18]. C_Q measures the interaction energy of Q and EFG tensors at the sites of quadrupole nucleus while η_Q measures the deviation of EFG tensors from cylindrical symmetry at the site of quadrupole nucleus. The nuclei with spin angular momentum greater than one-half ($I > 1/2$) are so-called quadrupole.

$$C_Q(\text{MHz}) = e^2 Q q_{zz} h^{-1} \quad (1)$$

$$\eta_Q = |(q_{xx} - q_{yy}) / q_{zz}| \quad (2)$$

RESULTS AND DISCUSSION

This work studies HB interactions properties of backbone

Table 1. The Geometrical Properties of 5NU^a

| | | | |
|---|--------|--|------|
| $r_{[\text{N-H}\dots\text{O1}]}$ | 2.01 Å | $\angle_{[\text{N-H}\dots\text{O1}]}$ | 170° |
| $r_{[\text{N-H}\dots\text{O1}]}$ ^b | 1.90 Å | $\angle_{[\text{N-H}\dots\text{O1}]}$ ^b | 167° |
| $r_{[\text{N-H}\dots\text{O2}]}$ | 2.01 Å | $\angle_{[\text{N-H}\dots\text{O2}]}$ | 167° |
| $r_{[\text{N-H}\dots\text{O2}]}$ ^b | 1.89 Å | $\angle_{[\text{N-H}\dots\text{O2}]}$ ^b | 163° |
| $r_{[\text{C-H}\dots\text{O3}]}$ | 2.23 Å | $\angle_{[\text{C-H}\dots\text{O3}]}$ | 169° |
| $r_{[\text{C-H}\dots\text{O3}]}$ ^b | 2.11 Å | $\angle_{[\text{C-H}\dots\text{O3}]}$ ^b | 166° |
| $r_{[\text{N}\dots\text{O1}]}$ | 2.89 Å | | |
| $r_{[\text{N}\dots\text{O2}]}$ | 2.87 Å | | |
| $r_{[\text{C}\dots\text{O3}]}$ | 3.16 Å | | |

^aData are from Ref. [13]. ^bAfter hydrogen optimization.

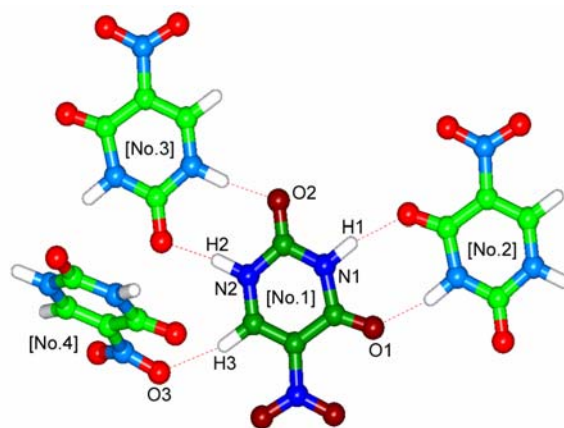


Fig. 1. The cluster model of crystalline 5-nitrouracil. Dash lines show hydrogen bonds (Table 1). The single model includes just one molecule [No.1].

uracil in 5NU by NQR parameters, C_Q and η_Q , which are evaluated by DFT calculations of the EFG tensors at the sites of ^{17}O , ^{14}N and ^2H nuclei (Table 2). To investigate the influence of HB interaction on the EFG tensors, the calculations were performed on one-molecule (single) and four-molecule (cluster) models of 5NU (Fig. 1). A quick look at the results of Table 2 reveals that the EFG tensors at the sites of various nuclei are differently influenced by HB interactions. The following text discusses the evaluated ^{17}O , ^{14}N and ^2H NQR parameters, respectively.

The ^{17}O NQR Parameters

Two oxygen nuclei of backbone uracil of the target

Table 2. The NQR Parameters

| Nucleus | Calculated ^a | | Literature ^b | |
|------------------|-------------------------|----------------|-------------------------|----------------|
| | C _Q (MHz) | η _Q | C _Q (MHz) | η _Q |
| ¹⁷ O1 | 10.7; 10.0 | 0.03; 0.16 | 7.85 (8.15) | 0.55 (0.61) |
| ¹⁷ O2 | 9.14; 8.25 | 0.23; 0.45 | 7.61 (8.48) | 0.50 (0.44) |
| ¹⁴ N1 | 3.69; 3.10 | 0.15; 0.51 | 2.60 | 0.52 |
| ¹⁴ N2 | 3.49; 2.92 | 0.10; 0.45 | 2.60 | 0.57 |
| ² H1 | 263; 238 | 0.15; 0.17 | - | - |
| ² H2 | 263; 238 | 0.17; 0.21 | - | - |
| ² H3 | 209; 198 | 0.04; 0.06 | - | - |

^aThe first number is for single model and the second number is for the target molecule in cluster. C_Q(²H) are in kHz. ^bAvailable NQR parameters of uracil are from Refs. [19,20] for oxygen and from Ref. [21] for nitrogen nuclei. The values in parentheses are calculated at the same level of theory of this study.

molecule contribute to N-H··O type of HB interactions with molecules numbers 2 and 3 in cluster model (Table 1 and Fig. 1). The amide type oxygen O1 interacts with N1 of molecule number 2 with intermolecular geometry properties of $r_{[N...O1]} = 2.89 \text{ \AA}$ and $\angle_{[N-H...O1]} = 167^\circ$. Due to this interaction, C_Q(¹⁷O1) decreases by 0.7 MHz and η_Q(¹⁷O1) increases by 0.13 from single model to cluster model. The urea type oxygen O2 interacts with N2 of molecule number 3 with intermolecular geometry properties of $r_{[N...O2]} = 2.87 \text{ \AA}$ and $\angle_{[N-H...O2]} = 163^\circ$. Due to this interaction, C_Q(¹⁷O1) undergoes a reduction of 0.89 MHz and η_Q(¹⁷O1) undergoes an increase of 0.22 from single model to the target molecule in cluster model. Since the chemical environments of the two oxygen nuclei of backbone uracil in 5NU structure are different, the observed changes of their NQR parameters due to HB interactions are also different. The more significant change of η_Q at the site of O2 compared to that of O1 indicates that, due to protection of -NO₂ group, the EFG tensors at the site of O1 are less oriented into arbitrary directions when contributing to HB interactions compared to those at the site of O2.

Parallel results are observed for change of C_Q values at the sites of O1 and O2 from single to the target molecule in cluster model. The more change of C_Q(¹⁷O2) compared to that of ¹⁷O1 indicates that O2 contributes to a stronger HB interaction than O1, referring to the protective role of -NO₂ group in 5NU

structure.

The ¹⁴N NQR Parameters

Similar to the number of oxygen nuclei, backbone uracil has two nitrogen nuclei which contribute to N-H··O type of HB interactions with molecules numbers 2 and 3 in the cluster model of 5NU. N1 interacts with O1 of molecule number 2 with intermolecular geometry properties of $r_{[N...O1]} = 2.89 \text{ \AA}$ and $\angle_{[N-H...O1]} = 167^\circ$. Due to HB interactions effects on the EFG tensors, C_Q(¹⁴N1) shifts 0.59 MHz to lower fields while η_Q(¹⁴N2) shifts 0.36 to upper fields from single to the target molecule in cluster model of 5NU. N2 contributes to HB interaction with O2 of molecule number 3 with intermolecular geometry properties of $r_{[N...O1]} = 2.87 \text{ \AA}$ and $\angle_{[N-H...O1]} = 163^\circ$. Hence, C_Q(¹⁴N2) decreases 0.57 MHz and η_Q(¹⁴N2) increases 0.35 from single to the target molecule in cluster of 5NU. Since the magnitude of change of NQR parameters at the sites of two nitrogen nuclei due to HB interactions is almost similar, it seems that the EFG tensors at the sites of these two nuclei do not feel the -NO₂ protection effects.

The ²H NQR Parameters

Three hydrogen nuclei of backbone uracil of the target molecule contribute to HB interactions through N-H··O and C-H··O types in 5NU. H1 is chemically bonded to N1 and

participates in N-H \cdots O type of HB interaction with O1 of molecule number 2 in cluster of 5NU with intermolecular geometry properties of $r_{[N-H\cdots O1]} = 1.90 \text{ \AA}$ and $\angle_{[N-H\cdots O1]} = 167^\circ$. $C_Q(^2H1)$ decreases 25 kHz and $\eta_Q(^2H1)$ increases 0.02 from single to the target molecule in cluster of 5NU. Because of poor electronic density at the sites of hydrogen nuclei, they are not accurately located by X-ray. Furthermore, since the EFG tensors are originated at the electronic sites of quadrupole nuclei, the C_Q at the sites of hydrogen nuclei is at the order of kHz while that of other nuclei is at the order of MHz. H2 is chemically bonded to N2 and interacts with O2 of molecule number 3 through N-H \cdots O type of HB interactions with intermolecular geometry properties of $r_{[N-H\cdots O2]} = 1.89 \text{ \AA}$ and $\angle_{[N-H\cdots O2]} = 163^\circ$. Although because of poor electronic density, the EFG tensors at the sites of hydrogen nuclei are less influenced by HB interactions compared to those of other nuclei, the small change of NQR parameters at the sites of hydrogen nuclei are not negligible.

Due to HB interaction, $C_Q(^2H2)$ decreases 25 kHz and $\eta_Q(^2H2)$ increases 0.04 from single to the target molecule in cluster of 5NU similar to those of H1. It has been observed in previous section that the change of NQR parameters at the sites of N1 and N2 due to HB interactions are equal, similarly, equal change of NQR parameters due to HB interactions at the sites of H1 and H2 nuclei which are respectively chemically bonded to N1 and N2 is observed here. H3 is the last hydrogen nucleus of backbone uracil in 5NU which interacts with O3 belonging to -NO₂ group of molecule number 4 through C-H \cdots O type of HB interactions with intermolecular geometry properties of $r_{[C-H\cdots O3]} = 2.11 \text{ \AA}$ and $\angle_{[C-H\cdots O3]} = 166^\circ$. Although this non-classical type of HB interactions is already expected as weak interactions, a significant change of NQR parameters at the site of H3 are observed. Due to participating in C-H \cdots O type of HB interaction, $C_Q(^2H3)$ decreases 11 kHz and $\eta_Q(^2H3)$ increases 0.02 from single to the target molecule in cluster of 5NU. The magnitude of change of NQR parameters at the site of H3 is less than those at the sites of H1 and H2; however, the observed change due to C-H \cdots O type of HB interactions is not still negligible.

Comparison of Results of This Study with Previous Ones on Uracil

In crystalline structure of uracil [19], the HB interactions

properties are completely different from what are seen in this work. In uracil, O1 contributes to N-H \cdots O type of HB interactions with two neighbor molecules and O2 contributes to C-H \cdots O type of HB interactions with two neighbor molecules. Wu *et al.* [20,21] have recently reported the ¹⁷O NQR parameters of uracil either experimentally or computationally. Because of different HB interaction properties between uracil and 5NU, the calculated NQR parameters of uracil at the same level of calculations are observed in lower fields in comparison with those of 5NU. Both nitrogen nuclei of uracil interact with O4 of neighbor molecules in crystalline structure; however, in 5NU, N1 interacts with O1 and N2 interacts with O2 of neighbor molecules.

Previously, Rabbani *et al.* [22] reported the experimental values of ¹⁴N NQR parameters. Since the HB interaction properties at the sites of two nitrogen nuclei are similar, equal parameters were reported for them. However, HB interactions properties are different at the sites of N1 and N2 in crystalline structure of 5NU and, therefore, different NQR parameters are calculated at the sites of these two nitrogen nuclei. It is noted that the C_Q parameters of nitrogen nuclei in uracil are still observed at lower fields rather than those of 5NU.

CONCLUSIONS

We studied HB interactions properties of backbone uracil in crystalline structure of 5NU by DFT calculations of ¹⁷O, ¹⁴N and ²H NQR parameters in two single and cluster models. The results indicated different HB interactions properties at the sites of various nuclei and also the protective role of -NO₂ group for O1 to contribute to HB interactions found to be weaker than O2. The NQR parameters at the sites of both of N1 and N2 are influenced with equal magnitude due to HB interactions; however, $C_Q(^{14}N2)$ is observed at lower fields compared to that of N1. Although the sites of hydrogen nuclei are low in electron density, the NQR parameters at these sites feel the changes due to HB interactions. Furthermore, contributing to C-H \cdots O type of HB interactions causes the NQR parameters at the site of H3 feel changes. Finally, comparison of the results of this study with those previously reported for uracil reveal that the HB interactions properties are almost different in these two crystalline structures.

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